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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,956	02/26/2004	Mary J. Bossard	SHE0081.00	5777

21968 7590 12/23/2004

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EXAMINER	
MONDESI, ROBERT B	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 12/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/789,956	BOSSARD ET AL.	
	Examiner	Art Unit	
	Robert B Mondesi	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *October 28, 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to restriction requirement

Applicant's election with traverse of Invention I, Claims 1-30 in the amendment, filed November 02, 2004 is acknowledged. The traversal is on the ground(s) that 3 of the 4 Groups of inventions are in the same search class and therefore it is not a search burden to search and examine the entire application. This is not found persuasive because even though the Groups are in the same general search class they are nonetheless directed towards divergent subject matter. Inventions of Groups III and IV are drawn to a method making and a method of treating, respectively, and are patentably distinct from each other and from the compositions of the inventions of Groups I and II, for the reasons mentioned in the Office action mailed November 02, 2004. Furthermore the product of the present invention is not presently allowable therefore processes of making and using the product of the invention cannot be rejoined.

Therefore the requirement is still deemed proper and is made FINAL. **Claims 1-62** are pending in this application. **Claims 31-62** are withdrawn from further consideration by the Examiner because these Claims are drawn to non-elected inventions. **Claims 1-30** are currently under examination.

Priority

The current application filed on February 26, 2004, claims priority to provisional application 60/450,578 filed on February 26, 2003.

Preliminary Amendment

The preliminary amendment filed July 26, 2004 has been entered.

Information Disclosure Statement

The IDS(s) filed October 28, 2004 and November 15, 2004 have been received and are signed and considered, a copy of the PTO 1449 is attached to the following document.

Specification

The disclosure is objected to because of the following informalities:

The use of the trademarks HEMOFIL, KOATE, MONARC-M, MONOCLATE-P, HELIXATE FS, KOGNATE FS, RECONBINATE, ADVANTE, REFACTO (Page 3, section 0007) have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is drawn to biologically active fragments of Factor VIII. The claim does not require that the polypeptide possess any particular conserved structure, or other distinguishing feature, such as a specific biological activity. Thus, the claim is drawn to a genus of polypeptides that is defined by an unclear functional relationship to Factor VIII. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in the claim that is sufficiently disclosed is a partial structure in the form of a recitation of percent identity. The specification does not identify any particular portion of the structure that must be characteristics of the claimed genus are not described. The only adequately described species is Factor VIII and no active variants are disclosed. Accordingly, the specification does not provide adequate written description of the claimed genus.
Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the a14 that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed." (See page 1117.) The specification does not it clearly allow persons of ordinary skill in the art to recognize that [he or she]

invented what is claimed." (See *Vas-Cath* at page 1116), As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers* v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird,* 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF' s were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Therefore, only Factor VIII, but not the full breadth of the claim meets the written description provision of 35 U. S.C. 112, first paragraph. Applicant is reminded that *Vas-cath* makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 12-15, 17-22, 24, 26-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Minamino et al. United states Patent 6,037,452 (cited in The IDS filed October 28, 2004).

Miniamino et al. disclose Factor VIII, Factor IX, Factor VIIIa, Factor IXa and analogous polypeptides covalently bonded through a bonded group to poly(alkylene oxide) (column 1, lines 61-64). Miniamino et al. disclose further that the invention is not only applicable to factor VIII and factor IX obtained from blood but also to Factor VIII and Factor IX manufactured by recombinant DNA procedures (column 3, lines 15-18). Miniamino et al. teach that the present invention is not limited to normal Factor VIII (i.e., bound to Factor VIII:vWF) and Factor IX, but also to Factor VIII:C and various active species of any of them, or inactive precursor species (whether of longer or shorter chain length than purified Factor VIII or Factor IX as obtained from blood fractionation) and the Factor VIII and Factor IX, as well as the various activated forms and analogous structures thereof (various analogous structures with deletion, substitution, addition, etc. of one or more amino acids, but retaining the Factor VIII and/or Factor IX biological activity can be prepared, especially through recombinant DNA procedures) as useful herein, should contain an amino terminus and a carboxyl terminus. In addition, linkage along the polypeptide chain or chains forming the same is generally of the amide type as is well known, with some modifications thereof through any intra or inter-chain bonding.

Miniamino et al. also teach that bonding of the poly(alkylene oxide) thereto can occur not only at terminal portions of the polypeptide, but also along the chain(s) thereof to form side-chains of poly(alkylene oxide) and it is believed that the linking most likely involves formation of covalent bonds using intermediate linking or coupling reagents; however, other types of bond formation are contemplated herein such as ionic bonds, van der Waals force bond, and so forth. Furthermore, the poly(alkylene oxide) can be modified so that only one terminus thereof can participate in the reaction with the peptide (whether or not through a coupling reagent) by preliminarily reacting the poly(alkylene oxide) with an alkyl group such as lower C.sub.1-5 alkyl, especially methyl or ethyl, to form the corresponding alkoxy groups. Other OH protecting or activating groups can be employed, for example, acyl such as propionyl or other lower acyl (C.sub.1-5) groups as other protecting groups or, for example, phenyl or alkyl-substituted phenyl groups can be employed. The protecting groups used herein include those known in the art.

Miniamino et al. teach further that most often, the poly(alkylene oxide) will react through a terminal hydroxyl group (the oxygen) or a modified terminal group such as, for example, when the terminal hydroxyl or hydrogen thereof has been replaced by another reactive moiety such as amino and the latter is especially useful where reaction is to be with carbonyl moieties of a linker or of the peptide itself and also known methods of forming an active derivative of the polyalkylene glycol can be employed herein such as the alkylation method, the acid azide method,

the diazo method, the condensation method, etc., which are then allowed to react with free amino or carboxyl groups in the peptide to effect bonding (Column 2-3, lines 15-67 and lines 1-13).

Miniamino et al. also dilscose modified Factor VIII in which there is a substituted 2,4-bis (methoxypolyoxy-ethylene)-6-triazine of which polyoxyethylene moiety has molecular weight of 5000 or more.

Thus Miniamino et al. teach all the elements of **Claims 1-7, 12-15, 17-22, 24, 26-30** and these claims are anticipated under 35 USC 102(b).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-4 and 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miniamino et al. United states Patent 6,037,452 in view of Davis et United States Patent 4,179,337 (cited in The IDS filed November 15, 2004).

Miniamino et al. disclose compositions comprising Factor VIII covalently bound to poly(ethylene oxides) as mentioned above.

Miniamino et al. do not disclose compositions comprising Factor VIII covalently bound to poly(ethylene oxides) with nominal molecular weight of 10,000 Daltons to 85,000 Daltons.

Davis et al. disclose biologically active molecules covalently bound to poly(ethylene oxides) with nominal molecular weight of 10,000 Daltons to 85,000 Daltons (column 2, lines 42-57). It would have been obvious to one of ordinary skill in the art at the time the invention was made to covalently bind Factor VIII to poly(ethylene oxides) with nominal molecular weight of 10,000 Daltons to 85,000 Daltons for the advantages reduced immunogenecity and increased bio-availability as taught by Miniamino et al. and Davis et al., see Miniamino et al. at column 1, lines 26-34 and Davis et al. at column 1, lines 15-50.

Claims 1, 3-4 and 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miniamino et al. United states Patent 6,037,452 in view of Greenwald United States Patent 5,298,643 (cited in The IDS filed November 15, 2004).

Miniamino et al. disclose compositions comprising Factor VIII covalently bound to poly(ethylene oxides) as mentioned above.

Miniamino et al. do not disclose compositions comprising Factor VIII covalently bound to poly(ethylene oxides) with nominal molecular weight of 53,000 Daltons to 75,000 Daltons.

Greenwald discloses biologically active molecules, including Factor VIII (Column 8, lines 33-37, covalently bound to poly(ethylene oxides) with nominal molecular weight of 10,000 Daltons to 85,000 Daltons (column 3, lines 51-54). It would have been obvious to one of ordinary skill in the art at the time the invention was made to covalently bind Factor VIII to poly(ethylene oxides) with nominal molecular weight of 53,000 Daltons to 75,000 Daltons for the advantages reduced immunogenecity and increased bio-availability as taught by Miniamino et al. and Greenwald, see Miniamino et al. at column 1, lines 26-34 and Greenwald at column 1, lines 17-29.

Claims 1,14 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rostin et al. in view of Greenwald United States Patent 5,298,643.

Rostin et al. disclose compositions comprising B-domain deleted Factor VIII covalently bound to poly(ethylene oxides) with nominal molecular weight of 5,000 Daltons (Materials and Methods, Pages 388-391).

Rostin et al. do not disclose compositions comprising B-domain deleted Factor VIII covalently bound to poly(ethylene oxides) with nominal molecular weight of higher than 5,000 Daltons.

Greenwald discloses biologically active molecules, including Factor VIII (Column 8, lines 33-37, covalently bound to poly(ethylene oxides) with nominal molecular weight of higher than 5,000 Daltons. (column 3, lines 51-54). It would have been obvious to

one of ordinary skill in the art at the time the invention was made to covalently bind Factor VIII to poly(ethylene oxides) with nominal molecular weight of higher than 5,000 Daltons for the advantages reduced immunogenecity and increased bio-availability as taught by Rostin et al. and Greenwald, see Rostin et al. at page 1, columns 1-2, and Greenwald at column 1, lines 17-29.

Claims 1, 23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miniamino et al. United states Patent 6,037,452 in view of Longenecker et al. United Stated Patent 4,994,439.

Miniamino et al. disclose compositions comprising Factor VIII covalently bound to poly(ethylene oxides) as mentioned above.

Miniamino et al. do not teach that the mentioned composition is lyophilized or further comprises a pharmaceutically acceptable excipient.

Longenecker et al. teach compositions comprising Factor VIII (Column 3, line55), polyethylene oxide (Example 3, column 11, line 10-11), a pharmaceutical excipient (examples 1-3) that are lyophilized (column 8, lines 61-67).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare lyophilized compositions comprising covalently bound Factor VIII to poly(ethylene oxides) and an excipient for the advantages of the ease of storage and administration as taught by Miniamino et al. and Longenecker et al., see Longenecker et al. at columns 1, lines 1-35.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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12-14-04

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